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Nicholas J. Seay
Quarles & Brady LLP
P O Box 2113
Madison, WI 57301-2113

EXAMINER	
SITTON, JEHANNE SOUAYA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)	
Office Action Summary	10/655,915	ATTIE ET AL.	
	Examiner	**Art Unit**	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 12* is/are pending in the application.

4a) Of the above claim(s) *4-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/4/2007 has been entered.

2. Currently, claims 1-8, and newly added claims 12 are pending in the instant application. Claims 4-8 are withdrawn from consideration as being drawn to a non elected invention. Claims 1-3 and 12 are currently under examination. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections are either newly applied, as necessitated by amendment, or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is Non-FINAL.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action..

Specification

4. The amendment filed 8/15/2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: In table 1, at page 4 of the specification, the amendment changes the amino acid position "50" to "52" for the Thr/Ile, B6/BTBR respectively. However, the specification does not provide support for this specific change. At page 12, first paragraph, the response asserts that this change was made to correct an "inadvertent misnumbering". This argument has been thoroughly reviewed but was not found persuasive. As set forth in the MPEP 2163 (I) (B): "While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure. An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also recognize the appropriate correction. In re Oda, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971)." In the instant case, the specification does not appear to provide guidance that the correct amino acid position is 52. While a threonine is present in the hSorCS1 amino acid sequence at position 52, threonine is also present at, for example, amino acid 68, as well as in the different mouse SorCS1 isoforms (see Figure 2). Accordingly, one skilled in the art, based on the guidance in the specification, would not have recognized the existence of the error or the appropriate correction.

Applicant is required to cancel the new matter in the reply to this Office Action.

Response to Arguments

5. The response traverses the rejection. The response asserts that one or ordinary skill in the art would readily recognize that none of the nucleotide sequences in the vicinity correlate with the nucleotides surrounding and at position 172. The response provides partial sequences of B6 and BTB1 SorcS1 cDNA and protein sequences to illustrate the difference of a T vs I at codon 52, and asserts that if the mouse cDNA is translated with the mutation of C to T at 172, this results in a thr to ile change at amino acid 52 of the mouse sequence. The response concludes that since the mouse cDNA in table 1 was based on a publicly available sequence, the ordinary artisan would have recognized the existence of the inadvertent error. These arguments have been thoroughly reviewed but were found unpersuasive. Although the response provides the nucleic acid partial sequences of SorCS1 for B6 and BTBR mice, these sequences were not provided in the specification, nor is there any evidence that either of these sequences were publicly available at the time the invention was filed. Further, the response provides no citation for any specific mouse SorCS1 cDNA sequence, nor any evidence that the sequence was publicly available at the time the invention was filed. Additionally, figure 2 specifically refers to position 50, not 52. Accordingly, the arguments are not persuasive to overcome the objection.

6. The amendment filed 5/4/2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: In table 1, at page 4 of the specification, the amendment changes the amino acid position from 1140 to 1139 and 1150 to 1149. Additionally,

the nucleotide sequences are changed from 3433 to 3436 and 3462 to 3465, respectively. However, the specification does not provide support for this specific change, nor does the specification provide any cDNA sequences for mouse isoforms SorCS1a, b, or c. At page 6, second paragraph, the response asserts that this change was made to correct a clerical error due to "inadvertent misnumbering". This argument has been thoroughly reviewed but was not found persuasive. As set forth in the MPEP 2163 (I) (B): "While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure. An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also recognize the appropriate correction. In re Oda, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971)." In the instant case, the specification does provide any cDNA sequences for murine SorCS1 or any of the isoforms a, b, or c. Although Figure 2 does provide amino acid sequences for murine Sorcs1a, b, and c isoforms, the 1139 to 1140 change is taught to occur in isoform a. Both positions 1139 and 1140 are taught to be Ser in the figure, however the figure provides absolutely no basis for changing the position from 1139 to 1140 and does not provide any nucleotide sequence whatsoever. Turning to the change from 1149 to 1150, which is taught to occur in isoform c, it is noted that position 1150 shown in figure 2 is E, not T. Additionally, figure 2 specifically references position 1149, not 1150. Additionally, no nucleic acid sequence is provided by the specification. The changes to the nucleotide numbering at 3462 to 3465 is not supported by the specification. Accordingly, one skilled in the art, based on the guidance in the specification, would not have recognized the existence of the error or the appropriate correction.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 2 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 12 are drawn to "Assessing whether a human subject is susceptible to type 2 diabetes comprising the step of determining the cDNA sequence of the subject [human] in the SorcS1 gene" wherein comparison to SEQ ID NO: 3 and a difference at nucleotide 172, indicates that the human subject is a candidate for type 2 diabetes. The designation of specific position 172 with reference to SEQ ID NO: 3 is unclear however, as position 172 of SEQ ID NO: 3 is a g, not a cytosine (or thymine).

Enablement

9. Amended claims 1-3 and newly added claim 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

Amended claim 1 is drawn to a method of assessing whether a human subject is susceptible to type 2 diabetes by determining the SorCS1 cDNA sequence of that subject, deducing the amino acid sequence encoded thereby, and comparing it with SEQ ID NO: 4, wherein a difference of a threonine to isoleucine substitution at amino acid position 52 of the SorCS1 amino acid sequence indicates that the subject is susceptible to developing type 2 diabetes. Amended claim 2, is drawn to a method of assessing whether a human subject is susceptible to type 2 diabetes by determining the cDNA sequence of the subject in the SorCS1 gene and comparing it with SEQ ID NO: 3, wherein a difference of a cytosine to thymine substitution at nucleotide position 172 of the SorCS1 cDNA sequence indicates that the subject is susceptible to developing type 2 diabetes. Amended claim 3 is drawn to a method of determining if a human being is a candidate for developing type 2 diabetes by determining the sequence of the protein coding region of the human SorCS1 gene in the genome of the human, deducing the amino acid sequence encoded by the region sequenced, and comparing the deduced amino acid sequence to SEQ ID NO: 4, wherein a difference of a threonine to isoleucine substitution at amino acid position 52 of the SorCS1 amino acid sequence indicates that the human being is a candidate for developing type 2 diabetes. Newly added claim 12 is drawn to a method of determining whether a human subject is a candidate for developing type 2 diabetes by determining the cDNA sequence of the subject in the SorCS1 gene and comparing it with SEQ

ID NO: 3, wherein a difference of a cytosine to thymine substitution at nucleotide position 172 of the SorCS1 cDNA sequence indicates that the human is a candidate for developing type 2 diabetes.

The nature of the invention, therefore, requires the knowledge of predictive associations between position 52 relative to SEQ ID NO: 4 or position 172, relative to SEQ ID NO: 3 or the "SorCS1" cDNA, and susceptibility to developing type 2 diabetes.

The claims recite "protein coding region" or "cDNA" of the SorCS1 gene, however it is known that in mice, different isoforms of SorCS1 exist. The specification does not teach the different isoforms of human SorCS1. Further, the designation of specific position 172 with reference to SEQ ID NO: 3 is unclear because position 172 of SEQ ID NO: 3 is a g, not a cytosine (or thymine). The specification does not teach any other SorCS1 cDNA sequence in humans.

The invention is in a class of inventions which the CAFC has characterized as 'the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)).

The specification teaches that the inventors began by narrowing the genetic region associated with severe type 2 diabetes to a 7 MB segment of mouse chromosome 19 (page 4, para 0017). The specification teaches that 2 genes previously found in the region were SorCS1 and SorCS3, which belong to a family sharing a large region of similarity including the VPS10 domain. The specification teaches that due to similarity with sortilin, SorCS1 and SorCS3 are expected to be involved in insulin-stimulated glucose transportation and in controlling body fat metabolism. The specification teaches that the 7MB region was characterized and that it was

found that the only difference between severely diabetic mice and less severely affected mice was 3 mutations in SorCS1, leading to 3 amino acid changes (table 1). The specification, however, does not teach the specific function or activity of SorCS1. The specification does not teach if other mutations occurred in other portions of the mouse genome that may be responsible for the severe form of diabetes observed in the mice.

The specification provides no teaching or working examples of any mutations in any portion of the SorCS1 gene in humans, or an association between SorCS1 alleles in a human subject and type II diabetes susceptibility. The specification asserts at page 3 that the SorCS1 gene in mice is "directly analogous" to the human gene, however this statement is unclear. The genes are not identical, and the meaning of "directly analogous" cannot be determined. For example, at table 1, the specification teaches different mutations at specific positions of mouse SorCS1. The specification teaches a mutation, at position 1140 from Ser to Phe, and at position 1150 from Ser to Pro. However, in humans position 1140 is Asp, and position 1150 (in SEQ ID NOS 4) is His. None of these amino acids are "directly analogous" to either amino acid found in mice at each position. Although, the specification has been amended to recite a mutation at position 52 from Thr to Ile (also found in SEQ ID NO: 4), the specification provides no teaching of the specific function or activity for SorCS1, or any of these 3 positions, accordingly the affect of each amino acid at such positions is unpredictable. Additionally, claims 1 and 3 broadly encompass any nucleotide change which leads to an isoleucine substitution at position 52, however only a single specific nucleotide substitution which leads to this alteration in mice is taught. The specification does not teach if the amino acid substitution is the causative mutation which leads to a more severe form of diabetes in mice, or if the nucleotide change may be in

linkage with another allele. Therefore, given the lack of guidance from the specification as to any mutations in any region of the SorCS1 gene in humans, a teaching of the function of SorCS1 including critical amino acids and domains required for function, or a predictable correlation between the presence of SorCS1 mutations and diabetes susceptibility in other species, the skilled artisan would be unable to predict an association between the claimed positions in the protein coding region or cDNA of the SorCS1 gene in humans and susceptibility to type 2 diabetes.

The specification's assertions with regard to putative SorCS1 activity is based on homology analysis with sortilin and the family of proteins that contains a VPS10 domain (page 4, end of para 00017). However, it is known for nucleic acids as well as proteins that even a single nucleotide or amino acid change or mutation can destroy or alter the function of a biomolecule in many instances, albeit not in all cases. The effect of these changes are largely unpredictable as to which ones have a significant effect verses not. The prior art does not teach the function of SorCS1 or how it is involved in type 2 diabetes. The post filing specifically date art provides some characterization of SorCS1 (see Hermey et al, JBC, vol. 278, Feb. 2003, pages 7390-7396), but teaches that neither the mature luminal domain nor any of the cytoplasmic domains of the different SorCS1 isoforms bound any of the ligands previously shown to interact with sortilin and SorLA, demonstrating sorCS1 is functionally different from the previously characterized Vps10-D family receptors (para bridging pages 7390-7391). Additionally, Hermey teaches that the different isoforms of SorCS1 have completely different cytoplasmic domains that mediate different trafficking in cells (abstract). It is clear that the art supports that SorCS1 has a different function than other Vps10 domain family members, and that the 3 different

isoforms of SorCS1 do not function in the same manner where the different cytoplasmic domain for each isoform mediates different trafficking in cells.

Claims 1-3 and 12 appear to be drafted based on the amended specification's recitation that a difference was found in the SorCS1 gene between B6 and BTBR mice corresponding to amino acid position 52. The specification asserts "It appears that the activity of the SorCS1 protein may determine islet mass. Alternatively, the SorCS1 protein may affect insulin secretion in pancreatic beta cells or insulin degradation in the kidney or liver" (page 8, para 00033), however the specification does not teach the function of SorCS1, or whether or how the change from Thr to Isoleucine altered the function or activity of the SorCS1 nucleic acid or protein such that the change provides an increased susceptibility to type 2 diabetes in mice. Accordingly, the affect of the mutation of Thr to Ile, is unpredictable in humans. The specification provides no guidance as to whether this mutation, or the other mutations listed in Table 1, occurs in a critical region or domain or how it affects the function or activity of a critical region or domain, such that the skilled artisan would be able to predict the same effects in humans. The specification provides no teaching or working examples that this mutation, or the other mutations listed in Table 1, exists in humans or would have a similar affect in humans. Kahn teaches that disruption of a specific gene in mouse models of diabetes does not necessarily provide a predictable correlation that any polymorphism in the corresponding human sequence would be similarly associated (Kahn, Cell, vol. 92, pages 593-596, 1998, cited in the IDS). Kahn teaches "Withers et al., reported that disruption of IRS-2 causes diabetes in mice. The most compelling aspect of this report is that inactivation of this single gene causes defects in both insulin action and insulin secretion." (page 593, last para of col. 2). However, Kahn further teaches "The parallels between the IRS-2 knockout mice and Type 2 diabetes in humans raises the tantalizing question as to whether human diabetes is

caused by mutations in the IRS-2 gene. Disappointingly, studies in press in several populations, including Danish Caucasians... reveal no association between polymorphisms in the IRS-2 gene and Type 2 diabetes" (page 594, 2nd full para in col. 2).

The instant specification provides no teaching or guidance as to the role of critical amino acids in any of the isoforms of either murine or human SorCS1 nor how such are involved in susceptibility to type 2 diabetes. The specification provides no predictable association that any alteration, in any protein coding region or cDNA of the SorCS1 gene, including those claimed, in humans, let alone any species, is diagnostic or indicates a susceptibility for developing type 2 diabetes. No predictable correlation between the structural alterations in the mouse sequence and susceptibility for developing type 2 diabetes has been taught by the specification. The specification does not teach the function of SorCS1 nor how it's function, or lack of function, or altered function are predictably associated with type 2 diabetes.

The quantity of experimentation in this area is extremely large as it requires analysis of claimed positions in the SorCS1 gene to determine whether the isoleucine variant at position 52 of SEQ ID NO: 4, or the nucleotide variant T, at position 172 of SEQ ID NO: 3, which would alter the Gly amino acid at codon 55 to valine, is associated with type 2 diabetes. As neither the art nor the specification provide guidance as to whether the amino acids at such positions are critical to the function of SorCS1 or are in some way associated with diabetes susceptibility such analysis is replete with trial and error experimentation, with the outcome being unpredictable.

In order to practice the invention as claimed, one would first have to establish that a predictive relationship exists between the disclosed mutations and susceptibility to type 2 diabetes in humans. Such experimentation could involve functional analysis of a protein whose

actual function has to be determined as well. The experimentation could also involve a large study of patients and controls to screen for mutations in SorCS1 in humans to determine whether the claimed mutations are associated with susceptibility to type 2 diabetes in humans. Such analysis represents an inventive and unpredictable undertaking with each of the many intervening steps not providing any guarantee of success.

Thus, given the broad claims in an art whose nature is identified as unpredictable, the state of the prior art, the lack of guidance in the specification, the breadth of the claims and the quantity of experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention commensurate in scope with the claims.

Response to Arguments

The response traverses the rejection. The response asserts that the specification sets forth at page 5, para 00019 that the genomic and cDNA sequences of mouse SorCS1 were known to those of skill in the art at the time of filing. This argument has been thoroughly reviewed but was not found persuasive as this statement could not be found in the paragraph indicated. The response further asserts that the degree of identity between the mouse and human SorCS1 coding region is sufficient to soundly predict that applicant's genetic evidence from the congenic mouse model is predictive of the same genetic phenomenon in humans and that the term 'directly analogous" is intended to mean that the mouse and human SorCS1 genes are similar in structure and function. At page 10, the response summarizes the teachings of the specification and concludes that applicants discovered the difference in susceptibility to diabetes resolved down to differences in the alleles of the gene for SorCS1, and that since the same correlation exists in mice also exists

in humans and since the corresponding homologous SorCS1 gene having a conserved threonine at amino acid position 52 is found in both mice and humans, the same susceptibility to developing type 2 diabetes is found in humans and in mouse. This argument has been thoroughly reviewed but was not found persuasive. Although figure 2 provides an alignment between the three isoforms in mice as well as human SorCS1, this alignment provides no analysis regarding regions or domains which are critical to activity or function. The genetic background of the congenic mice and humans would not be expected to be the same. It is not clear, from the teachings in the specification, whether the mutations disclosed in the specification are the cause for the difference in diabetes susceptibility between the B6 and BTBR mice, or whether one or more of the mutations act in concert with or are linked to the causative mutation which could be hundreds or thousands of nucleotides away in a different gene or on a different chromosome. It is not clear from the teachings of the specification, or the assertions in the response, that the only difference in the mice genetically, was that leading to the 3 amino acid differences in table 1, or that the Thr to Ile mutation occurred at position 52. It is additionally unclear, and the specification does not teach whether the Thr to Ile change provided for a difference in activity or function of SorCS1, to establish a predictive association between this amino acid change and T2D in any genetic background. The specification provides no correlation between the structure of the specific mutation in Table 1 and their affect on the function or activity of SorCS1 to provide for T2D susceptibility. With regard to the assertion that "since the same correlation that exists in mice also exists in humans, and since the analogous SorCS1 gene having a conserved Threonine at amino acid residue 52 is found in mouse and humans, the same susceptibility to developing T2D should be found in humans and in mouse", it

is noted that the meaning of "the same correlation exists in mice also exists in humans" is unclear, because it is not clear which "correlation" is being referred to. The response at page 11, also asserts that "among the genes analyzed in mice, SorCS1 is the only gene which applicants detected ... expression level differences. In fact, applicants believe that these expression differences cause the increased diabetes risk". These arguments have been thoroughly reviewed but were found unpersuasive. The specification does not appear to disclose any expression levels differences detected for SorCS1, nor does it provide any guidance that the mutations disclosed in table 1 led to expression level changes. Accordingly, these arguments are not persuasive. Additionally, such argument is considered Attorney's arguments and cannot take the place of evidence on the record. As stated in the MPEP, 2106 "Arguments of Counsel"

"However, it must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See In re Budnick, 537 F.2d at 538, 190 USPQ at 424; In re Schulze, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); In re Cole, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement."

With regard to SorCS1 function, at page 9, the response reiterates the teachings of para 00033 of the specification, and asserts "Specifically, it is believed the reduced or altered insulin levels in the congenic mice are a result of a decreased insulin secretion in vivo, which is associated with disrupted islet morphology. Furthermore, it is noted that the cellular function of SorCS1 is still unknown, however it is known to bind platelet growth factor-BB. This growth factor is required for the recruitment of pericytes or their precursor to vascular endothelial cells, where they stabilize the microvasculature and have a key role in blood vessel development. Maintenance of proper islet vasculature is important for both insulin secretion and islet survival and thus may be of particular relevance to the mammalian phenotype disclosed in the instant

specification." This argument has been thoroughly reviewed but was unpersuasive to overcome the rejection. First, the instant specification has provided no teaching of the specific function of SorCS1 other than speculation on it's activity with regard to islet mass or alternatively it's affect on insulin secretion or insulin degradation (para 00033). None of the mutations disclosed are discussed with regard to such function, nor is any guidance provided by the specification on the affect of such mutations with regard to the possible functions disclosed in the specification and asserted to in the response. Second, it is further noted that the specification does not teach these assertions made in the response. These assertions are considered attorney's arguments and cannot take the place of evidence on the record.

Written Description

10. Amended claims 1-3 and newly added claims 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended claim 1 is drawn to a method of assessing whether a human subject is susceptible to type 2 diabetes by determining the SorCS1 cDNA sequence of that subject, deducing the amino acid sequence encoded thereby, and comparing it with SEQ ID NO: 4, wherein a difference of a threonine to isoleucine substitution at amino acid position 52 of the SorCS1 amino acid sequence indicates that the subject is susceptible to developing type 2 diabetes. Amended claim 2, is drawn to a method of assessing whether a human subject is susceptible to type 2 diabetes by

determining the cDNA sequence of the subject in the SorCS1 gene and comparing it with SEQ ID NO: 3, wherein a difference of a cytosine to thymine substitution at nucleotide position 172 of the SorCS1 cDNA sequence indicates that the subject is susceptible to developing type 2 diabetes. Amended claim 3 is drawn to a method of determining if a human being is a candidate for developing type 2 diabetes by determining the sequence of the protein coding region of the human SorCS1 gene in the genome of the human, deducing the amino acid sequence encoded by the region sequenced, and comparing the deduced amino acid sequence to SEQ ID NO: 4, wherein a difference of a threonine to isoleucine substitution at amino acid position 52 of the SorCS1 amino acid sequence indicates that the human being is a candidate for developing type 2 diabetes. Newly added claim 12 is drawn to a method of determining whether a human subject is a candidate for developing type 2 diabetes by determining the cDNA sequence of the subject in the SorCS1 gene and comparing it with SEQ ID NO: 3, wherein a difference of a cytosine to thymine substitution at nucleotide position 172 of the SorCS1 cDNA sequence indicates that the human is a candidate for developing type 2 diabetes.

The amended claims are drawn to "Assessing whether a human subject is susceptible to type 2 diabetes comprising the step of determining the protein coding region [cDNA sequence] of the human SorcS1 gene" wherein comparison to SEQ ID NO: 4 or 3 respectively and a difference at amino acid 52 or the nucleic acid 172, respectively, indicates that the human subject is a candidate for type 2 diabetes. However, the specification provides no basis for these specific nucleotide or amino acid positions in humans.

At para 00020 of the specification, the specification generally sets forth diagnostic use for examining humans for their SorCS1 gene and determining differences with respect to SEQ ID

NO: 4. Although the specification recites specific positions in Table 1, these positions are with regard to differences found in B6 vs BTBR mice, both of which, were diabetic, albeit with differing severity. However, the specification does not appear to set forth diagnostic methods for diabetes susceptibility in humans by determining any *particular* mutation or position. Accordingly, the newly added claims directed to diagnostic methods in humans at a specific SorCS1 position appears to introduce new matter into the instantly claimed invention.

Additionally, as the mutations disclosed were found in mice not in humans, there is no evidence that such mutations would even exist in any human SorCS1 nucleic acid or protein sequence. The designation of specific position 172 with reference to SEQ ID NO: 3 is further unclear. Position 172 of SEQ ID NO: 3 is a guanine, not a cytosine (or thymine). The specification does not teach any other SorCS1 cDNA sequence, let alone any sequences with mutations, in humans.

With regard to the recitation of amino acid "52", in table 1, at page 4, the specification was amended to change the amino acid position from "50" to "52" for Thr/Ile, B6/BTBR respectively. However, the specification does not appear to provide support for this specific change. At page 12, first paragraph, the response asserts that this change was made to correct an "inadvertent misnumbering". However, as set forth in the MPEP 2163 (I) (B): "While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure. An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also recognize the appropriate correction. In re Oda, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971)." In the instant case, the specification does not appear to

provide guidance that the correct amino acid position is 52. While a threonine is present in the hSorCS1 amino acid sequence at position 52, threonine is also present at, for example, amino acid 68, as well as in the different mouse SorCS1 isoforms (see Figure 2). Given the limited guidance in the specification, it does not appear that one of skill in the art would not have recognized the existence of the error or the appropriate correction. The arguments with regard to the specification objection are not persuasive for the reasons made of record above.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton
Primary Examiner
Art Unit 1634

7/23/07